

## Chapter 5, Version 1.0

### The Planning Year: The Center Application

The results of your partners meeting and strategic planning process should be of substantial assistance as you prepare the AP4 center grant application, which is the final task of the planning year. Many sections of the application will be based on the results of your strategic planning, so application writer(s) should participate in the center strategic planning team meetings to keep abreast of developments in the plan. Allow plenty of time—ideally several months—to prepare, review, and have others review your application.

Basic AP4 center requirements are described in Chapter 1, and preparation of the AP4 center planning application is described in Chapter 2. Some of that information is repeated here so this chapter can provide, in a single place, a complete description of the AP4 center application content and format. This chapter also describes proposed review criteria (due to be updated in 2004) for the center application and some tips on writing a successful grant application.

#### Requirements of the AP4 Program

The NCI developed the AP4 initiative in 2003 to bring together multidisciplinary expertise among academia, nonprofit institutions, industry, and government entities needed to discover new, more effective cancer interventions, shorten the time required to bring the interventions to clinical trials, and reduce the financial risks of cancer intervention discovery and development.

Only successful recipients of an AP4 center planning grant may apply for an AP4 center grant. However, receipt of an AP4 planning grant does not guarantee that any subsequent application for an AP4 center will be approved.

**Figure 5-1: Required components of AP4 centers**

- Center director at a U.S. university or nonprofit organization.
- Multidisciplinary research teams.
- Research projects designed to culminate in clinical interventions.
- At least two biotechnology, pharmaceutical, academic, nonprofit, and/or state and local government partners.
- Membership fees of at least \$300,000 a year from partners.
- A steering committee with representatives of each partner organization.
- A membership agreement.
- Patent coverage.
- Annual formal evaluations of projects and the AP4 center.
- Annual reports.

The NCI plans to award up to six 5-year grants to establish AP4 centers. Although the NCI currently plans to support this program, awards under the AP4 center RFA are contingent on the availability of funds and the receipt of enough meritorious applications. It is not known whether this RFA will be reissued.

AP4 centers with a combined partnership investment of at least \$450,000 per year will receive \$600,000 (direct costs) from the NCI in each of the first 3 years. Centers with a *minimum* of \$300,000 per year (total) from center partners will receive \$450,000 per year (direct costs) from the NCI in Years 1-3. Indirect costs will be allocated at the customary rate negotiated with the Department of Health and Human Services. Funding will be 75% of the initial direct cost

level in Year 4, and 50% of the initial direct cost level in Year 5, to encourage centers to acquire

additional contributing partners and prepare to become self-sustaining. Successful AP4 centers can compete for a second 5-year award of \$100,000–\$200,000 (direct costs) per year. After 10 years, centers that continue to operate must be fully supported by industrial, nonprofit, and other (non-NIH) federal and/or state and local government partners.

Features of each AP4 center will include:

- A center director located at the U.S. academic or nonprofit institution hosting the AP4 center. The center director conceives of the idea for the AP4 center, applies for the planning grant, coordinates planning-year activities, and, if successful in the subsequent center application, oversees all aspects of the center. The center director also consults with center partners to define a research agenda focused on shared research interests, needs, and opportunities.
- Multidisciplinary participation from such fields as chemistry, biology, immunology, and screening technologies.
- Research projects of interest to the cancer research community. All center research should emphasize new technologies and be designed to develop new anticancer therapeutic, preventive, diagnostic or imaging agents, and to culminate in clinical trials. The center application should showcase at least three projects for the initial year of funding, with clear evidence of criteria for go/no-go decisions and evidence of the ability to develop new projects over the entire funding period. Projects must focus on “orphan” cancers (those that affect fewer than 200,000 people per year in the United States) or biologically defined subsets of more common tumor types. At least two additional projects should be included in the AP4 center application as back-up projects in the event that the steering committee terminates one or more initial projects early in the center's life cycle.
- At least two biotechnology, pharmaceutical, academic, nonprofit, and/or state and local government partners that contribute financially to center operations. Ideally, the partners have nonoverlapping or complementary interests.
- A minimum of \$300,000 a year in total annual membership fees from center partners.
- A steering committee with representatives from each partner organization that approves activities and recommends new projects in response to evolving opportunities. The NCI program coordinator serves as a nonvoting member of this committee. The steering committee meets twice a year to review and approve the initiation, continuation, or discontinuation of research projects.
- A membership agreement signed by all partners that addresses how the center is governed, as well as the management of intellectual property issues, publication procedures, partnership fees, and definition of the terms of royalty-free, nonexclusive licenses to partners. The agreement must follow the NIH Data Sharing Policy (available at: [http://grants1.nih.gov/grants/policy/data\\_sharing/index.htm](http://grants1.nih.gov/grants/policy/data_sharing/index.htm)) to address the sharing of easily transferable research findings.

- Development of scientific expertise in research relevant to cancer intervention discovery and development at the academic level.
- A strong research team capable of developing and operating an AP4 center.
- Patent coverage. Because the discovery of new cancer interventions is the goal of the AP4 center, and active involvement by entities other than the academic or nonprofit institution will be facilitated by adequate patent coverage, AP4 center applicants must provide plans to ensure such coverage. Patent coverage could be complicated because multiple institutions will be involved. Each center must therefore provide a detailed description of its approach for obtaining patent coverage and for licensing when appropriate, especially when the invention may involve investigators from more than one institution. Procedures must be described for resolving any legal problems that may arise. This information must be included in the membership agreement. Patent coverage is addressed by P.L. 96-517, as amended by P.L. 98-620 and 37 CFR Part 401. Instructions on patent coverage have been published in the *NIH Guide for Grants and Contracts*, Vol. 19, Issue 23, June 22, 1990.
- Annual formal evaluations of the partnership compiled by an independent evaluator (see Chapter 9) who works with the center director but is independent of the center. The evaluator provides survey and analysis information to the center director and partners to continually improve the center. He or she reports on the center evaluation process at each steering committee meeting, and solicits feedback on the progress of each project. The evaluator is also responsible for preparing, on an annual basis, a review of center activities, including:
  - Status of collaborations.
  - Participant satisfaction with center activities.
  - Center management and operation.
  - Exit surveys from partners who have withdrawn from the center.
- Annual reports prepared by the AP4 director that are submitted to the NCI program coordinator. Each report should address major accomplishments, operating budget, evaluation results, research goals, and processes used to communicate with center partners.
- Facile access to the development contract resources of the NCI Developmental Therapeutics Program (DTP) (formulation, bulk synthesis, pharmacology, toxicology) for promising lead compounds approved by the steering committee and that meet NCI criteria for interest.
- Investigational New Drug (IND) filing assistance through the Cancer Therapy Evaluation Program (CTEP) for an NCI-based clinical trial or a principal investigator-based trial on a case-by-case basis. This may involve assistance in putting together INDs that are held by the originating center or assumption of the IND if the agent is to be studied more broadly in NCI's early clinical trials groups.

### **Funding Mechanism**

The administrative and funding instrument used for the AP4 grant is a cooperative agreement (U54), which is an assistance mechanism (rather than an acquisition mechanism) in which the NCI is actively involved in scientific and/or programmatic activities. Under the cooperative agreement, the NCI

supports and/or stimulates the recipient's activities by serving as a partner but does not direct or have a dominant role in the activities. The center's home institution has the dominant role in, and prime responsibility for, center grant activities.

### ***Center Director Rights and Responsibilities***

The center director has primary authority and responsibility for defining objectives and approaches. She/he has responsibility and accountability to the academic or nonprofit institution and to the NCI for performance and proper conduct of activities supported by the AP4 center grant, in accordance with the terms and conditions of award.

### ***NCI Staff Responsibilities***

NCI participates as a partner in the AP4 center and is represented by an NCI coordinator—a scientist from the NCI extramural staff who participates as a member of the steering committee, interacts scientifically with the center, and facilitates the role of NCI as a center partner. During the award period, NCI may provide assistance by participating in the design of activities, and advising in the selection of resources, staff, etc., and on management and technical performance. In all cases, the role of NCI will be to facilitate but not to direct activities.

An NCI program director will have standard program stewardship responsibilities for this award.

### ***Collaborative Responsibilities***

The AP4 center grant is overseen by a unit consisting of a center director, principal investigators, their respective programs, and an NCI coordinator. Foreign institutions may participate as partners in the center, but not as awardee institutions, and their scientists may not serve as center directors.

### **Preparing the AP4 Center Application**

A small group should be assigned to help prepare the AP4 center grant application. This group should include some strategic planning team members because the application must be closely linked to the strategic plan. In addition to one or two center investigators and partners, the group should include someone from the host institution's research office. One member of the application group should be responsible for addressing such issues as patent policy, publication delays, membership fees, and cost

sharing with appropriate host institution officials.

#### **Figure 5-2: Tips for completing the PHS 398 application form**

1. Read the PHS 398 application instructions very carefully (available at: <http://grants.nih.gov/grants/funding/phs398/phs398.html>).
2. Read the RFA very carefully.
3. Meticulously follow instructions for the PHS 398 form and the RFA.
4. Read the NCI's Quick Guide for Grant Applications (available at: <http://deainfo.nci.nih.gov/EXTRA/EXTDOCS/gntapp.htm#2>). It provides many helpful tips for the main sections of the PHS 398 form.
5. Spell out all acronyms on first use.
6. Use basic English and avoid jargon.
7. Include graphs, tables, and figures only when they complement the text and are essential to the narrative.
8. Have someone outside the proposed AP4 center read the application for clarity and consistency.
9. Proofread the application carefully; do not rely on spell-check to catch all errors.

Establish deadlines for completing sections of the grant application, especially if several individuals are involved in its preparation. Keep in mind any institutional deadlines that could delay completion of the application, and allow time for equipment breakdowns, competing responsibilities of those preparing the application, and

other potential sources of delay.

Once the group decides what to cover in the application, each member should take responsibility for drafting a section or sections; these should be distributed to other group members for comment. If possible, a grant writer should ensure that all sections are completed on time and all comments are integrated. The grant writer should then edit the application for consistency and completeness. Alternatively, the center director can draft the entire application and then distribute it to group members for comment.

As soon as a draft is available, it should be reviewed by individuals outside the application group, including some who are not involved in the center. Be sure to proofread the document several times, as this is often required to catch all errors and inconsistencies.

### Application Content

The AP4 center application must include a list of committed partners and a detailed description of how the partners will communicate and how decisions will be made. Support from the NCI for AP4 centers is considered seed funding to develop a partnership among industry, academic institutions, nonprofit organizations, and government agencies, with NCI serving in an advisory capacity. As described above, a significant proportion of a center's support is expected to come from industrial, academic, nonprofit,

and state and local government partners. As a center progresses, it is likely to have increased opportunities for funding from other firms and other federal, state, and local governments.

The center application should reflect the unique combination of the proposing institution's research interests, capabilities, and potential for working with multidisciplinary partners. These features should be discussed in sufficient detail to facilitate review in accordance with AP4 requirements.

The NCI recommends that those submitting an AP4 center application follow the outline below.

#### 1. *Introduction*

In no more than three pages, describe the technical focus of and need for the center. This section should describe:

- Research focus (an orphan disease affecting fewer than 200,000 people per year in the United States or a biologically defined subset of more common tumor types).
- The current state of research in this area.
- Expertise and resources that will be used to address this need.

#### 2. *Center Structure and Operations*

Address the following administrative issues:

- Evidence of institutional involvement and participation.

#### Figure 5-3: Application content

- Introduction: the technical focus of and need for the center.
- Center structure and operations.
- Research plan.
- Financial management.
- Attachments:
  - A list of individuals who will participate in the center.
  - Biographical sketches of key center participants.
  - Current and pending support for key participants.
  - Proposed membership agreement document.
  - A list of center partners and their letters of financial commitment or intent.
  - A list of additional collaborating institutions
  - Evaluation metrics.

- Available facilities and infrastructure.
- A director responsible for all center activities, with evidence of the director's management capability beyond research experience.
- Intellectual property policies that may be in accordance with the Bayh-Dole Act that permit nonexclusive, royalty-free licenses for center partners and the possibility of exclusive, royalty-bearing licenses; where departure from Bayh-Dole provisions is planned, this should be specifically noted and agreed to in the membership agreement and by institutional representatives.
- Publication rights policies.
- Center membership fee structure, roles of center partners, and specific membership benefits.
- A proposed evaluator and plans for how the center will meet AP4 center evaluation requirements.

### 3. *Research Plan*

For each of the three or more proposed initial research projects, describe (in no more than 3 pages per project):

- Names and capabilities of investigators.
- Project goals, relevance, and time scale.
- Involvement of students and the steering committee in planning and executing the project, if applicable.
- Available research facilities.
- Project budget.

Also provide brief (1-page) descriptions of at least two back-up projects, which may be needed if the steering committee terminates one or more initial projects early in the center's life cycle.

### 4. *Center Financial Management*

The center application should include a separate budget detailing all costs, including funds to support the independent evaluator. The initial-year budget should provide details on annual center support from the partners. The application must include a proposed budget for each of the 5 years of center operation and a summary budget for all 5 years.

### 5. *Attachments*

- A list of key individuals and other participating individuals. The list should identify institutional and departmental affiliation or discipline for each individual and five publications that are most relevant to the proposed research. The application should include biographical sketches of the center director and all key center investigators or individuals from other institutions who will be directly involved in center development, operation, and evaluation.
- Current and pending support for key individuals who are requesting salary support from the NCI.
- The proposed membership agreement document.
- A list of participating center partners and their letters of financial commitment or intent.

- If applicable, a list of collaborations from additional (non-partner) institutions that details their level of involvement and fees generated. Note that interinstitutional collaborations are possible and encouraged.
- Each potential center should determine evaluation metrics for each project and the center (see Chapters 7 and 9) and include these in the center application. Sample metrics questions include:
  - Was the high-throughput assay qualified and implemented satisfactorily?
  - Was a cancer-relevant target characterized?
  - Was a method for analyzing output from a new screen identified and successfully used to select compounds of interest?
  - Have there been as many new candidates identified for intervention development as anticipated?
  - Have center partners continued to communicate and contribute to center operations?
  - How many patents or Investigational New Drug Applications have been filed?

### **Format of the AP4 Center Grant Application**

The AP4 center application must be submitted on the Public Health Service (PHS) 398 form, available at most institutional offices of sponsored research; from the Division of Extramural Outreach and Information Resources, National Institutes of Health, 6701 Rockledge Drive, MSC 7910, Bethesda, MD 20892-7910, telephone 301-435-0714, e-mail: [grantsinfo@nih.gov](mailto:grantsinfo@nih.gov); and on the Internet at <http://grants.nih.gov/grants/funding/phs398/phs398.html>.

Instructions for the AP4 center application have been modified to reflect NIH's streamlining "just-in-time" effort. According to the just-in-time concept, applicants may wait to submit certain information until it is clear that an award may be granted. This concept was implemented to reduce the administrative burden on applicants, reviewers, and NCI staff.

PHS 398 grant application instructions are available electronically on the [grants.nih.gov](http://grants.nih.gov) website in rich text file (RTF) and portable document file (PDF) format. RTF files can be opened and altered with most common word processors. In addition, many word processing programs allow users to save a document in RTF when they select "save as...." However, changes to PDF versions of the form can only be saved on computers with certain types of Adobe Acrobat software, such as Adobe Acrobat Professional.

The [grants.nih.gov](http://grants.nih.gov) website provides detailed instructions on completing the PHS 398 application form and examples of some sections of the form. Before you begin writing the grant application, carefully read the instructions for the PHS 398 and the RFA for the AP4 center, and become familiar with all necessary requirements and certifications. You should also read the instructions on implementing an AP4 center in Chapters 6–9 of this handbook. In addition, ask colleagues for copies of successful NIH grant applications to gain a more concrete idea of what each section should include. Incomplete applications will be returned without review.

**Note: The summary in this section of certain key components of the PHS 398 form is intended to show you how to use the PHS 398 form to describe your plans for an AP4 center grant. These instructions are NOT intended to substitute for reading all of the RFA and PHS 398 instructions carefully.**

The PHS 398 form includes the following sections:

***Form Page 1: Face Page***

- Project title.
- RFA title: Academic Public Private Partnership Program (AP4) Grant.
- RFA number: To be determined.
- Center director name and address.
- Dates and total costs of AP4 center project.
- Signatures of center director and applicant organization representative.

***Form Page 2: Description, Performance Sites, and Key Personnel***

- Abstract that describes succinctly every major aspect of the center, except budget.
- Performance site.
- List of key personnel, including center evaluator.

***Form Page 3: Research Grant Table of Contents***

- Page numbers of each application section.

***Form Page 4: Detailed Budget for Initial Budget Period***

All amounts must be in U.S. dollars. List only the direct costs requested in this application. For each person who will be involved in the proposed AP4 center during the initial year (including all applicant organization employees, collaborating investigators, individuals in training, and support staff), regardless of whether a salary is requested, list the following:

- Name.
- Role in the AP4 center.
- Number of months per year in the individual's appointment to the applicant institution.
- Percent of effort on AP4 center activities.
- Institutional base salary.
- Salary requested.

Also list costs in the initial year of the center for:

- Consultants.
- Equipment.
- Supplies.
- Travel.
- Alterations and renovations.
- Other expenses.

***Form Page 5: Budget for Entire Proposed Period of Support***

Enter totals under each budget category for all additional years of requested support. Identify with an asterisk (\*) any significant increases or decreases from the initial-year budget. Also, justify budgets with more than a standard escalation from the initial to future year(s) of support.



Each budget item listed on Form Page 4 must be clearly justified beginning at the bottom of Form Page 5. In the budget justification section (which has no page limit), address:

- Specific functions of *all* personnel by position, role, and level of effort. This includes consultants and to-be-appointed positions.
- Appointments that are less than full time (identify these with an asterisk on Form Page 4).
- Any significant increases or decreases in Years 2–5 from the initial-year budget (identify these with an asterisk on Form Page 4).
- Any salary requests that are less than a multiple of the individual's institutional base salary and the percent of effort in the center.
- Services to be performed by all consultants.
- Travel requests.
- Alterations and renovations.
- Other expenses.

***Biographical Sketch Format Page*** (each biographical sketch may not exceed four pages)

- Name.
- Education/training.
- Positions and honors.
- Selected peer-reviewed publications or manuscripts in press (in chronological order).
- Research support.

***Resources Format Page***

- Computer resources.
- Office space.
- Major equipment.

***Research Plan*** (limit of 25 pages for sections a–d)

- a. Specific aims (1 page recommended). Could include goals and objectives outlined in the strategic plan. These should address types of cancer(s) targeted by the proposed AP4 center, types of research and training planned, roles of center partners, and center administration.
- b. Background and significance (2–3 pages recommended). Could address the center director, other investigators, and partners, and the background and significance of the proposed center's research focus.
- c. Preliminary studies/progress report (6–8 pages recommended). Could address other activities by investigators and/or partners relevant to the proposed AP4 center projects, resources provided by potential partners, and experience of the center director, other investigators, and partners.
- d. Research design and methods (13–16 pages recommended). Describe how specific aims will be accomplished through the center's research, training, partnership, and other activities. Provide an evaluation plan. Include 3-page descriptions of at least three initial research projects and 1-page descriptions of at least two back-up projects.
- e. Human subjects research. Address the involvement of human subjects and protections from research risk relating to their participation in the proposed research plan. Either justify an exemption from coverage by human subjects regulations, or address all six required points.

- f. Vertebrate animal research. Describe the proposed use of vertebrate animals as it relates to work outlined in the research plan. If your research involves vertebrate animals, you must address five points in this section.
- g. Literature cited (6-page limit).
- h. Letters from potential partners.

***Resources Page***

Describe resources, facilities, and support available to center researchers. Additional pages may be attached to the form.

***Checklist Form Page***

- Application type.
- Program income.
- Assurances/certifications.
- Facilities and administrative costs.
- Smoke-free workplace.

***Personal Data Form Page***

- Center director's race and ethnicity.

***Other Support Format Page***

- List active and pending support for center director and key personnel.

When the application is ready, affix the RFA label available in the PHS 398 form to the bottom of the application's face page. If you do not use this label, it might not reach the review committee in time for review. The RFA label is also available at: <<http://grants.nih.gov/grants/funding/phs398/label-bk.pdf>>.

Submit a signed, typewritten original of the application, including the checklist and three signed photocopies, in one package to:

Center for Scientific Review  
National Institutes of Health  
6701 Rockledge Drive, Room 1040, MSC 7710  
Bethesda, MD 20892-7710  
Bethesda, MD 20817 (for express/courier service)

At the same time, send two additional copies of the application to:

Referral Officer  
National Cancer Institute  
6116 Executive Blvd, Room 8041, MSC 8329  
Bethesda, MD 20892-8329  
Rockville, MD 20852 (for express/courier service)

Applications may no longer be hand delivered to the NCI, except by courier services (i.e., FedEx, UPS, DHL, etc.).

Applications must be received on or before the anticipated due date of June 2005, or approximately 1 year after award of the planning grants. If an application is received after that date, it will be returned without review. Although receipt of an application is not immediately acknowledged, the NCI generally notifies applicants of the review and funding assignment within 8 weeks.

### **Review Criteria**

Upon receipt, applications are reviewed for completeness by the NIH and for responsiveness by the NCI. Incomplete and/or nonresponsive applications are returned to the applicant without further consideration.

All applications that are complete and responsive to the RFA are evaluated for scientific merit, in accordance with the review criteria below, by a peer review group convened by the NCI. The reviewers base their reviews in part on whether the research approach takes advantage of the latest technologies, allowing the center to change the way molecules and other intervention technologies are discovered and developed. As part of the review process:

- All applicants receive a written critique of their applications.
- Only applications deemed to have the highest merit—generally the top half of the applications under review—are discussed and assigned a priority score.

The goals of all NIH-supported research are to advance understanding of biological systems, improve the control of disease, and enhance health. In their written comments, reviewers will discuss specific aspects of the application (see Figure 5-4) to judge the likelihood that the proposed AP4 center will have a substantial impact on the pursuit of the NIH goals.

**Figure 5-4: Review criteria for AP4 center applications**

- Significance.
- Approach.
- Innovation.
- Investigators.
- Environment.

The peer review group will consider all criteria in assigning the application's score. As of the publication date of Version 1.0 of this chapter, review criteria for the AP4 center application are not finalized. Each successful planning grant applicant will receive the RFA, including the review criteria, for the AP4 center grant application. Possible criteria include:

#### *Significance*

- Do initial research projects address an orphan disease (affecting fewer than 200,000 people per year in the United States) or a biologically defined subset of a more common tumor type?
- Does the application propose new partnerships or new projects for existing partnerships?
- What effect will the potential AP4 center have on concepts or methods that drive this field?

#### *Approach*

- Are the conceptual framework, design, methods, and analyses adequately developed, well integrated, and appropriate to center aims?
- Does this application bring together sufficient expertise to implement an effective AP4 center?
- Do letters of financial commitment from AP4 center partners support center priorities and objectives?
- Does the application demonstrate the ability to complete the outlined research within the 5-year grant period?

- Are the research projects designed to culminate in the selection of candidate interventions for use in a clinical trial?
- Does the application provide evidence of adequate resources (space; personnel, including the center evaluator; protected time for research; funding)?

#### *Innovation*

- Does the proposed AP4 center involve novel concepts, approaches, or methods?
- Are the aims original and innovative?
- Will the center's research challenge existing paradigms or develop new methodologies or technologies?

#### *Investigator*

- Does the center director have strong scientific and administrative leadership ability?
- Are the roles of other researchers appropriate to their qualifications and experience?
- Does the center organization reflect management plans, staffing, budget, and operational procedures that are adequate for the center's success?
- Are initial projects appropriate to the experience level of the center director and other researchers (if any)?
- Do researchers involved in the AP4 center represent an appropriate range of disciplines?

#### *Environment*

- Does the scientific environment in which the proposed work will be done contribute to the probability of success?
- Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements?
- Is there evidence of strong institutional commitment and support?

The application does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a high priority score. For example, a center director may propose an approach to research that is not innovative but is essential to achieving one of the AP4 center goals.

#### **Next Steps**

As soon as you have received notification of an award, make final preparations to establish your AP4 center. The steering committee should hold its initial meeting to launch the research program. The center director should finalize all administrative details, partner membership agreements, and arrangements with center investigators. Additional information about implementing a new AP4 center is provided in Chapters 6–9.

#### **References**

National Cancer Institute. Quick Guide for Grant Applications. Available at: <http://deainfo.nci.nih.gov/EXTRA/EXTDOCS/gntapp.htm#2>. Accessed May 14, 2003.